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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,707	10/27/2005	Masataka Kuwana	4439-4036	2198

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EXAMINER	
DUTT, ADITI	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
05/02/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/549,707	KUWANA ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-16,19,20 and 22* is/are pending in the application.

4a) Of the above claim(s) *9-16,19,20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7 February 2008 has been entered.

Status of Claims

2. The amendment filed on 7 February 2008 has been entered into the record and has been fully considered.

3. Claims 2-8 are amended. Claims 9-16, 19-20 and 22, are withdrawn by Applicant. Claims 17-18 and 21 are canceled.

4. Claims 2-8, drawn to a monocyte-derived multipotent cell expressing CD14, CD34, CD45 and type I collagen, are being considered for examination in the instant application, are under consideration in the instant application.

Response to Amendment

Withdrawn objections and/or rejections

5. Upon consideration of the Applicant's amendment, all claim objections and rejections, not reiterated herein have been withdrawn, as overcome by cancellation and/or amendment of claims (7 February 2008).

6. Owing to redundancy, rejection under 35 U.S.C. § 103 is withdrawn.

Applicant's response pursuant Interview

7. Based upon the discussions in the interview dated 16 January 2008, Applicants assert that the claims were amended to incorporate a process step describing the preparation of MOMC, wherein the monocytes are obtained by culturing PBMCs on fibronectin. Applicants also submitted the recent publication citing differences between PSC and MOMC. Furthermore, to avoid potential 112, second paragraph issues for the use of "is able to", Applicants amended the claims to recite "capable of differentiating", citing MPEP to show that "capable" or "incapable" is not vague and indefinite as per MPEP guidelines.

8. Applicant's amendments and submission of the requested publication are fully considered and acknowledged. Applicant's claim amendments to include the process steps as mentioned above are considered, however, the process steps are not found to be related to the claimed product, which is "multipotent cells". The product-by-process claims do not recite the process of making the claimed multipotent cells,

rather describe the making of the predecessor of these cells, i.e. monocytes. Furthermore, Applicant's citing of the MPEP 2173.05(g) to assert the validity and finiteness of the term "capable" is misconstrued and inappropriate. It is to be noted that the term "capable" is not setting the boundaries because "capable" means, "is able", not necessarily "will do"; while "incapable" as in the MPEP citation, is a more definitive description, therefore, "capable" unlike "incapable" comprises open language. Thus, Applicant's insertion of the process steps to recite "capable of differentiating" does not provide specific functional characteristics of the claimed product and, therefore, does not demonstrate a distinction of the claimed MOMC over the PSC cells of Zhao et al.

Claim Rejections - 35 USC § 102

Rejection maintained

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 2-8 are rejected under 35 U.S.C. 102(b) as clearly anticipated by Zhao et al., (PNAS 100: 2426-2431, 2003).

10. The claims are directed to a monocyte-derived multipotent cell (MOMC) that expresses CD14, CD34 and CD45, type I collagen, wherein the cell is capable of differentiating into osteoblast, skeletal myoblast, chondrocytes, adipocytes, neurons, endothelial cells and mesodermal cells.

11. Zhao et al. teach the isolation of pluripotent stem cells from human peripheral blood monocytes, that resemble fibroblasts and express the monocytic and hematopoietic cellular differentiation stem cell markers, such as CD14, CD34 and CD45 (pages 2427-2428, Table 1). Zhao et al. further teach that human peripheral blood cells containing monocytes, when cultured under specific conditions, differentiate into macrophages, lymphocytes, epithelial, neuronal, endothelial and hepatocytes etc. (pages 2428-2430). However, as evidenced in Stem Cells (NIH, June 2001, pages 32-35), monocytes, macrophages, lymphocytes etc., are cells that belong to the mesenchymal or mesodermal family and, therefore, this limitation is inherent in the teachings of Zhao et al. Furthermore, although the reference is silent on the expression of collagen type I, this would be an inherent characteristic because the cells are derived from monocytes isolated from the peripheral blood mononuclear cells. Thus, Zhao et al. clearly anticipate the claimed invention.

Applicant's Response:

12. Applicant argues that the claimed MOMC are not the same as Zhao et al's PSC, and alleges that the Examiner has wrongly derived the conclusion that they are. Arguing over the semantics of the terms "identical" and "similar" usage to compare the cells, Applicants assert that many cells are similar in the field of molecular biology, however, "has nothing to do with being identical". Applicants allege that the Examiner has used improper hindsight to arrive at the conclusion.

13. To provide proof that the Zhao cells are different from the instant MOMC, Applicant demonstrates data showing that MOMC cultured under Zhao conditions do not differentiate to neurons, hepatocytes, or epithelial cells. Applicant further alleges that Zhao results were not reproducible, because Applicant did not obtain the same result as provided in the publication with regards to CD34 expression levels and the number of fibroblast like cells. Lastly, Applicant summarizes by asserting that "a clear difference in differential abilities of MOMC and PSC" exist as Zhao cells do not differentiate into osteoblasts, skeletal myoblasts, etc. and are not obtained by culturing PBMCs in vitro on fibronectin, as shown by MOMC. Applicant therefore concludes the PSC of Zhao do not anticipate the claimed MOMC, and Zhao et al do not disclose each and every element of the claims. Applicants submit a Declaration under 37 C.F.R. § 1.132 by

Masataka Kuwana, MD, Ph.D. along with a review article, providing data to support the above contention.

14. Applicant's Declaration and arguments, are fully considered and acknowledged, however, are not found to be persuasive. It is to be noted that the Declaration is not dated, therefore, is not compliant under 37 C.F.R. § 1.132. However, even if it would have been compliant, the Declaration is not persuasive because of the following reasons. Applicant is reminded that the claims read as product-by-process claims, and as set forth in MPEP Chapter 2113:

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Therefore, product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. As explained earlier, the method steps recited in the instant claims neither relate to the claimed multipotent cells, nor imply any structural limitations to the product. Moreover, MOMC and PSC cells are structurally similar and express the same markers as claimed, and additionally are multipotent or pluripotent stem cells having the potential of differentiation to various cell

lineages, and are certainly **capable** of differentiating into the claimed cell types under appropriate culture conditions (emphasis added). Furthermore, the publication submitted by Applicant (Seta and Kuwana) provides evidence that PSC and MOMC are structurally the same because both cell types express CD14, CD34 and CD45 (Table 1). Because the expression of type I collagen is indicated as "N/D" and not "-" (N/D is not defined in the article) for PSC, Examiner interprets N/D as not determined; that is, not tested. That the references (Zhao and Seta) are silent on the positive expression of collagen type I, does not prove otherwise, absent evidence to the contrary.

15. Furthermore, as evidenced by Blau et al. (Cell, 105: 892-841, 2001), adult stem cells and progenitor cells are not unique and compartmentalized to differentiation to specific cell types expressing specific markers. Blau et al further teach that stem cells can give rise to various cell lineages and tissues depending on the microenvironmental cues, growth factors, differentiation factors, etc., by virtue of plasticity, heterogeneity and transdifferentiation characteristics (Figs 1, 7, 8). For example neural stem cells can form skeletal muscle, bone marrow derived stem cells can form multiple tissues, and cells from various tissues can give rise to bone marrow cells (page 837, para 1). Hence PSC of Zhao et al and the instant MOMC, both being multipotent or pluripotent stem cells, both having derived from the same source and expressing the same markers, is capable of the same differentiation function. By the same

token, Applicant's argument that the examiner's conclusion with reference to He et al, is based upon improper hindsight reasoning, is inappropriate, because Zhao's PSCs are the same as the claimed product as explained above. Moreover, it must be recognized that any judgment on inherency is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

16. Furthermore, Applicant's results using the Zhao et al. medium to demonstrate that PSC is different from MOMC, is expected because Zhao et al cells are not grown on fibronectin, which can lead to distinct differentiation patterns as explained above. Additionally, as evidenced by Kim et al. (Regeneration and Transplantation, 13: 1185-1188, 2002; Fig 3), different expression and differentiation of mesenchymal stem cells to neuroprogenitor cells, are observed with different growth factors and substrates, fibronectin resulting in maximal response. Nonetheless, as stated above, Zhao's PSC are structurally the same as MOMC, therefore, the cells of the prior art would be functionally the same under identical culture conditions, absent evidence to contrary. Applicant's data do not support such information and, therefore, is inconclusive..

New Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

17. Claims 2-8 are rejected under 35 U.S.C. 102(a) and (e) as clearly anticipated by Reid et al., (US Patent Application Publication No. 2002/0182188 A1, with a prior filing date of 19 January 2000, application number 09/487,318).

18. Reid et al teach isolated progenitors or pluripotent cells from the human liver that express cell markers such as CD14, CD34, CD45 and collagen type I, wherein the hepatic progenitor cell contains mesenchymal, and hematopoietic progenitor cells, having the capacity to differentiate to various cell types like macrophages, lymphocytes, granulocytes, hepatic stellate cells, cartilage cells, bone cells, to name a few (abstract; page 5, para 0042; claims 18, 22 and 23; para 0001). As the liver progenitor cell is a pluripotent cell expressing the same markers as the claimed multipotent cells, the cells of the prior art anticipate the claimed invention.

Conclusion

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

21. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

22. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649

AD
24 April 2008